Amendments to the Specification:

Please amend paragraph 22 on page 9 of the substitute specification filed July 27, 2001 (a copy of which was resubmitted August 15, 2005) as shown below:

[022] LEGEND FOR FIGURE 2 in EXAMPLE 6: Inhibition of growth of small cell lung carcinoma cells in vitro by anti-Recognin antibody. The inhibition is proportional to the concentration of anti-Recognin, which was 50% effective in the picogram per cell range. Each bar in the Figure represents the mean +/-SD for 24 wells, that is, from 3 wells for each of eight separate preparations of anti-Recognin at each dilution. METHODS. Small Cell Lung carcinoma cell line UCHNCU, grown in suspension and maintained in RPMI 1640 10% FCS (fetal calf serum) was seeded in 96 well microtitre plates (round bottom) at 104 cells per well. Serial dilutions were made of anti-Recognin antibody which had been purified by adsorption to immobilized malignin so that final concentration of anti-Recognin in RPMI Fes was 116 to 1/1458; final total volume per well was 200 microlitres. Plates were incubated at 37°C in 6% CO_2 / air for 3 days. On day 3, cultures were pulsed with 1 uci/well tritiated thymidine (3HTdR~~)~~ for 6 hours), then cultures were harvested with automatic cell harvester on filter pads. Filters were dried for 2 hours in 37°C dry incubator, discs were placed into scintillation vials, 2 ml ~~Optiphase~~ OPTIPHASE scintillant added, tubes capped cpms counted on Beckman ~~LS 1800 beta counter~~ LS 1800 BETA COUNTER and % Inhibition calculated as Control-Experimental / Control x 100.

Please amend paragraph 24 on page 10 of the substitute specification filed July 27, 2001 (a copy of which was resubmitted August 15, 2005) as shown below:

[024] LEGEND FOR FIGURE 3 in EXAMPLE 7. Increase in concentration of serum anti-Recognin (antimalignin) antibody with age in individuals without tumors, and in human clinical breast cancer; and its return to normal after successful treatment. Each data point represents the mean (+/- standard deviation) concentration of antimalignin antibody. "N" indicates the number of specimens per data point. "Age in years, Normal Non-Tumor": specimens from normal

individuals without benign or malignant tumors: from the left, the first five points are one for each decade of age from the 3rd through the 7th; the sixth point is for ages 71-90. The 7th through 10th points represent 4 clinical states. 7th point: "Benign Breast Ox (Diagnosis)" - patients with a variety of mammographic anomalies judged benign on cytopathological examination; 34/35 were in the normal range of antibody concentration (135 ug/ml) (see text for discussion of "false positive" results). 8th point: "Breast Cancer at Dx (Diagnosis)": patients at time of diagnosis of breast cancer; these were all in the elevated range (135 or > ug/ml). 9th and 10th points: "Post Rx" data are 0.1 to 1 year, and 2 to 27 years respectively after successful treatment of breast cancer. The ages in years (mean+/-SD) of the patients for the 7th through 10th points were respectively 47.3(+/-11), 56.2(+/-12), 51.0(+/-11), and 53.2(+/-13). METHODS: 2,194 specimens were received at random from centres in the US and 2 in the UK. Determinations were performed blind in three independent laboratories. All specimens were collected in unsiliconized ED #6440 VACUTAINER ~~vacutainer~~ tubes (Becton ~~Dickensen~~ Dickinson Co.), the sera shipped in dry ice and determined blind within 24 hours by reacting 0.2 ml of serum with immobilized malignin in duplicate as previously described (see legend for Table in EXAMPLE 2).

Please add the following new paragraphs and Example headings after paragraph 32 on page 14 of the substitute specification filed July 27, 2001 (a copy of which was resubmitted August 15, 2005).

EXAMPLE 12

Production of Purified MALIGNIN Product from Crude MALIGNIN-Containing Fraction

[033] A crude malignin-containing fraction is prepared in accordance with the protocol provided in Examples 3 and 4 of U.S. Application Serial No. 07/744,649, filed August 8, 1991. The product MALIGNIN is further isolated from contaminants of the crude fraction using thin layer gel (TLG) chromatography as follows:

[034] The apparatus used is the commercially available one designed by Boehringer Mannheim GmbH; Pharmacia Fine Chemicals and CAMAG (Switzerland). The resin is 2.5 g of SEPHADEX G-200 superfine prepared in 85 ml of 0.5 M NaCl in 0.02 M $Na_2HPO_4KH_2PO_4$

Phosphate Buffer pH 6.8 (6.6-7.0). Allow to swell two or three days at room temperature with occasional gentle mixing. (Magnetic and other stirrers should not be used). The swollen gel is stabilized for three weeks at refrigerator temperatures; however, bacterial and fungal growth may interfere with the swollen gel. If the gel is to be kept for longer periods of time, a small amount of a bacteriostatic agent should be added (sodium Azide 0.02%). 2.5 g. of dry gel are used to make two 20 x 20 cm. glass plates of 0.5 mm. thick. The plates are either allowed to dry at room temperature for 10 minutes and transferred to a moist chamber where they can be stored for about two weeks, or they are used immediately after appropriate pre-equilibration. (Usually during the night for a minimum of 12 hours). The main function of equilibration is to normalize the ratio between the stationary and mobile phase volumes. With the pre-equilibrated plates in a horizontal position, substances to be determined are applied with micro-pipettes as spots or as a streak at the start line. 10 ml. to 20 ml. of 0.2-2% protein solution is placed on the edge of a microscopic cover slide (18 by 18 mm.) and held against the gel surface. In a few seconds the solution will soak into the gel. All samples are first prepared on the cover slides and then quickly applied. If not enough material is used, it is difficult to locate individual spots after separation. If too much material is applied no defined separation occurs. The samples are diluted with buffer for easier handling and the separation of samples is carried in a descending technique with the plate at an angle of 22°. The flow rate of about 1-2 cm/hour is most suitable. Marker substances (such as cytochrome C, hemoglobin, myoglobin or bromophenol blue labeled albumin) are applied at different positions across the plate and also to serve as reference proteins for calculation of relative distance (mobility) of unknowns. After application of samples, the plates are replaced in the apparatus and the paper wick pushed slightly downwards to ensure good contact with the gel layer. The paper wick must not drip. Excess moisture is wiped off. The liquid solvent in the reservoir is kept constant at 1 cm. from the upper end of the vessel. The runs are usually completed in 4 to 7 hours depending on the progress of separation. With colored substances separation follows directly. The separated spots of protein are easily made visible by transferring them to a paper sheet replica of the TLG plate after the chromatographic separation has been completed, and by staining them on the prewashed methanol + H_2O + acetic acid – 90:5:5, for 48 hours. The paper sheet is 3 mm. filter paper. A sheet of paper 20 x 18 cm. is placed over the gel layer and pressed (rolled) just enough to ensure contact with the gel. Care is

taken not to trap air under the paper (replica) and not to disturb the gel layer. The liquid phase is soaked off from the gel layer by the paper and removed after about one minute, immediately dried in an oven at 60° temperature for 15 minutes and stained in the normal way with any of the routine staining procedures. Staining is performed by spraying the replica-paper with 0.03% diazotized sulfanilic acid in 10% Sodium Carbonate (Pauley's Reagent). Staining can also be accomplished with a saturated solution of Amido Black in Methanol-Acetic acid (90:10 v/v is used); the staining time is 5-10 minutes. For destaining, rinse with two volumes of the 90:10 methanol and acetic acid solution mixed with one volume of H_2O. It is difficult to obtain low background staining without very extensive washing. The plates themselves may also be dried at about 60°C (in an oven with air circulation) but only if the MALIGNIN is to be stained. For isolation purposes, the plate should only be air dried at room temperature. Over-heating can lead to cracking, but this can usually be avoided with a 50° – 60°C temperature which dries a SEPHADEX G-200 plate in 15-30 minutes. The dry plates are allowed to swell for 10 minutes in a mixture of methanol + H_2O + acetic acid (75:20:5) and stained in a saturated Amido Black in the same solvent system for five hours and subsequently washed by bathing for two hours in the same solvent before they are dried. For molecular weight determinations, the distance from the starting line to the middle of each zone is measured with an accuracy of 0.05 mm. either directly on the print (replica) or on the densitogram. The result is expressed by the R_m value defined as the ratio of the migration distance of the tested protein (d_p) to that of cytochrome C or myoglobin (d_m) which is used as the reference protein: Relating migration distance of tested substance to standard is the formula ($-R_m = d_p/d_m$). A straight calibration line is obtained by plotting the logarithm of the molecular weight of the standards used against the R_m. From this line, the molecular weight of the unknown protein can be obtained. For most exact results mix equal parts of the protein sample solution with standard, in this case cytochrome C, before applying to the plate.

[035] In the above-described TLG step, the product MALIGNIN is observed as a discrete spot at a distance of approximately 0.91±0.02 with reference to the standard cytochrome C, yielding an approximate molecular weight of 10,000 for MALIGNIN.

[036] The product MALIGNIN, which has been produced at this stage, is soluble in distilled water, soluble at neutral or acid pH, and insoluble at alkaline pH and having a

spectrophotometric absorption peak of 280 mu. It is a polypeptide with molecular weight of approximately 10,000.

[037] The molecular weights of MALIGNIN produced in fermentation cultures stabilized in successive generations of the cultures as shown by the thin layer gel chromatography determination are set forth in Table Example 12 below. The reproducibility of the molecular weight determination is remarkable in view of the inherent limitation of TLG chromatography.

TABLE Example 12

Reproducibility of Molecular weight of MALIGNIN produced

Run No.	Mol. Wt.	Run No.	Mol. Wt.	Run No.	Mol. Wt.
1	9,500	9	10,100	17	10,180
2	8,900	10	10,180	18	10,190
3	10,000	11	10,180	19	10,190
4	10,050	12	10,180	20	10,180
5	10,100	13	10,180	21	10,000
6	10,000	14	10,050	22	9,500
7	10,150	15	10,180	23	10,180
8	12,500	16	10,190		

[038] MALIGNIN'S covalently linked amino acids are shown by hydrolysis with 6N HCL then quantitative determination to have the following average composition of amino acids:

Amino Acid	**Approximate Number of Residues**
Aspartic acid	9
Threonine	5
Serine	5
Glutamic acid	13
Proline	4
Glycine	6
Alanine	7

Valine	6
½ Cysteine	1
Methionine	2
Isoleucine	4
Leucine	8
Tyrosine	3
Phenylalanine	3
Lysine	6
Histidine	2
Arginine	5
Approximate Total	**89**

[039] The molecular weight of MALIGNIN as determined by repeat Thin Layer Gel chromatography was about 10,000. The molecular weight of MALIGNIN as determined by calculation using the amino acid composition set forth above is 10,067 or about 10,000 upon rounding.

EXAMPLE 13

Production of RECOGNIN M

[040] Malignant cells grown in tissue culture, a mammary carcinoma cell line designated MCF-7 were obtained from Mason Research Institute, Rockville, Maryland.

[041] Approximately 1 gm of packed cells of MCF-7 was not further propagated upon receipt but extracted immediately and Recognin was produced according to the protocol used for producing MALIGNIN from glioma cells set forth in Examples 3 and 4 of U.S. Application Serial No. 07/744,649, filed August 8, 2009. Thus, the entire medium plus cells was transferred to centrifuge tubes with cold 0.005 M phosphate buffer, pH 7, and centrifuged at 3,000 rpm in the cold for 10 minutes, the medium discarded, the cells washed twice with cold buffer, centrifuged again twice as before, and the washings discarded. The washed cells were suspended in the same buffer and disrupted by sonification for 20 seconds. The cell residues were

centrifuged at 30,000 rpm for 30 minutes, the solubilized protein in the supernatant decanted and collected, and the cell residues sonified twice more, until no further appreciable protein was solubilized. The solubilized protein was concentrated and the Recognin cloven and purified by CELLEX D (BioRad) and SEPHADEX 200 (Pharmacia) gel chromatography. The yield, molecular weight, amino acid composition, behavior on thin layer gel chromatography and immunological properties of this polypeptide is similar to those of MALIGNIN as described above in Example 12. The yield in the case of MCF-7 cells was approximately 1 mg/g wet weight of cells.

[042] The covalently linked amino acids of Recognin M are shown, by hydrolysis (in vacuo) with 6N HCL at 108°C for 12 hours followed by quantitative automatic determination, to have the following average composition of amino acids (the nearest integer for the mole number of each amino acid is the average of two separate determinations):

Amino Acid	**Approximate Number of Residues**
Threonine	5
Serine	5
½ Cysteine	1
Methionine	1
Valine	6
Isoleucine	4
Phenylalanine	3
Lysine	6
Histidine	2
Arginine	5
Aspartic acid	9
Glutamic acid	11
Leucine	8

Tyrosine	2
Proline	4
Glycine	9
Alanine	9
Approximate Total	**90**

[043] The molecular weight of Recognin M as determined by Thin Layer Gel chromatography was about 8,000. The molecular weight of Recognin M as determined by calculation using the amino acid composition set forth above is 9,870 or about 10,000 upon rounding.